SECUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Thomas Ciossek, Axel Ullrich, Birgit

Millauer

(ii) TITLE OF INVENTION: METHODS FOR DIAGNOSIS AND TREATMENT

10

OF MDK1 SIGNAL TRANSDUCTION DISORDERS

(iii) NUMBER OF SEQUENCES:

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: Lyon & Lyon

(B) STREET: 633 West Fifth Street

(C) CITY: Los Angeles (D) STATE: California

(E) COUNTRY: USA (F) ZIP: 90071

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: 3.5" Diskette, 1.44 Mb

(B) COMPUTER: IBM compatible

IBM P.C. DOS (Version 5.0) WordPerfect (Version 5.1) (C) OPERATING SYSTEM:

(D) SOFTWARE:

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER: to be assigned

(B) FILING DATE: January 3, 1995

(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

Prior applications total, including application

described below:

none

(A) APPLICATION NUMBER:

(B) FILING DATE:

(viii) ATTORNEY/AGENT INFORMATION:

(A) NAME: Warburg, Richard J.

(B) REGISTRATION NUMBER: 32,327

(C) REFERENCE/DOCKET NUMBER: 208/007

104 208/007

(ix) TELECOMMUNICATION INFORMATION:

(A)	TELEPHONE:	(213) 489-1600
(B)	TELEFAX:	(213) 955-0440
(C)	TELEX:	67-3510

(1) INFORMATION FOR SEQUENCE ID NO: 1:

(i)	SEQUENCE	CHARACTERISTICS:

(A) LENGTH: 4304

(B) TYPE: nucleic acid
(C) STRANDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: nucleic

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

AAGCGGCCGG	TCTGCAGTCG	GAGACTTGCA	GGCAGCAAAC	ACGGTGCGAA	50
CEAACCGGAG	GGGGGAGAGA	GAAATCAAAC	AGCTAAGCGT	GGAGCAGACG	100
GCTGGGACC	CAGAAGGGGA	TCGATGCGAG	GAGCGCAATA	ATAACAACAA	150
TAATAACCCA	CTTCGGAGCA	AACAGCATCT	AAAGAGCTGC	GACCCAACTG	200
CAGCCTAAAA	AAATCAAACC	TGCTCATGCA	CCATGGTTGT	TCAAACTCGG	250
TECCTTCGT	GGATTATTTT	GTGTTACATC	TGGCTGCTTG	GCTTTGCACA	300
CACGGGGGAG	GCGCAGGCTG	CGAAGGAAGT	ACTATTACTG	GACTCGAAAG	350
CACAACAAAC	AGAATTGGAA	TGGATTTCCT	CTCCACCCAG	TGGGTGGGAA	400
GAAATTAGTG	GTTTGGATGA	GAACTACACT	CCGATAAGAA	CATACCAGGT	450
GTGCCAGGTC	ATGGAGCCCA	ACCAGAACAA	CTGGCTGCGG	ACTAACTGGA	500
TTTCTAAAGG	CAACGCACAA	AGGATTTTTG	TAGAATTGAA	ATTCACCTTG	550
AGGGATTGTA	ATAGTCTTCC	CGGAGTCCTG	GGAACTTGCA	AGGAAACGTT	600
TAATTTGTAC	TATTATGAAA	CAGACTACGA	CACCGGCAGG	AATATACGAG	650
AAAACCTTTA	TGTTAAAATA	GACACCATTG	CTGCAGATGA	AAGTTTCACA	700
CAAGGTGACC	TTGGTGAAAG	AAAGATGAAG	CTGAACACTG	AGGTGAGAGA	750
GATTGGACCT	TTGTCCAAAA	AGGGATTCTA	TCTTGCCTTT	CAGGATGTAG	800
GGGCTTGCAT	AGCATTGGTT	TCTGTCAAAG	TGTACTACAA	GAAGTGCTGG	850

ACCATTGTTG	AGAACTTAGC	TGTCTTTCCA	. GATACAGTGA	CTGGTTCGGA	900
ATTTTCCTCC	TTAGTCGAGG	TCCGTGGGAC	ATGTGTCAGC	AGTGCCGAGG	950
AAGAGGCAGA	AAATTCCCCC	AGAATGCATT	GCAGTGCAGA	AGGAGAGTGG	1000
CTAGTACCCA	TTGGAAAATG	CATCTGCAAA	GCAGGCTATC	AGCAAAAAGG	1050
GGACACTTGC	GAACCCTGTG	GCCGCAGGTT	CTACAAATCT	TCCTCTCAGG	1100
ATCTCCAGTG	TTCTCGTTGT	CCAACCCACA	GCTTCTCTGA	CCGAGAAGGA	1150
TCATCCAGGT	GTGAATGTGA	AGATGGGTAC	TACAGAGCTC	CTTCTGATCC	1200
ACCATACGTT	GCATGCACGA	GGCCTCCCTC	TGCACCACAG	AACCTTATTT	1250
TCAATATCAA	TCAAACGACT	GTAAGTTTGG	AATGGAGTCC	TCCGGCTGAC	1300
AACGGGGGAA	GAAACGATGT	CACCTACAGA	ATACTGTGTA	AGCGGTGCAG	1350
TTGGGAACAG	GGAGAATGTG	TGCCATGCGG	AAGTAACATT	GGATACATGC	1400
CCCAGCAGAC	GGGATTAGAG	GATAACTATG	TCACTGTCAT	GGACCTACTT	1450
CCCATGCAA	ATTACACTTT	CGAAGTTGAA	GCTGTAAATG	GAGTTTCGGA	1500
CTTAAGCAGA	TCCCAGAGGC	TCTTCGCTGC	TGTTAGCATC	ACCACCGGTC	1550
AAGCAGCTCC	CTCGCAAGTG	AGTGGAGTCA	TGAAGGAGCG	AGTACTGCAG	1600
CGGAGTGTGC	AGCTTTCCTG	GCAGGAGCCG	GAGCATCCCA	ATGGAGTCAT	1650
CACGGAATAT	GAAATCAAGT	ATTATGAGAA	AGATCAACGG	GAAAGGACGT	1700
ACTCAACACT	CAAAACCAAG	TCCACCTCCG	CCTCCATTAA	TAATCTGAAA	1750
CCGGGAACAG	TGTACGTCTT	TCAGATCCGG	GCGGTCACTG	CTGCCGGTTA	1800
IGGAAACTAC	AGCCCTAGGC	TTGATGTTGC	CACACTTGAG	GAAGCTTCAG	1850
GTAAAATGTT	TGAAGCGACA	GCAGTCTCCA	GTGAACAGAA	TCCTGTCATC	1900
ATAATTGCTG	TAGTGGCTGT	AGCAGGGACC	ATCATCTTGG	TGTTCATGGT	1950
GTTCGGCTTC	ATCATTGGAA	GAAGGCACTG	TGGTTATAGC	AAGGCTGACC	2000
AAGAAGGGGA	TGAAGAACTC	TACTTTCATT	TTAAATTTCC	AGGCACCAAA	2050
ACCTACATTG	ACCCTGAAAC	CTATGAGGAC	CCAAATAGAG	CTGTCCATCA	2100
ATTCGCCAAG	GAGCTAGATG	CCTCCTGTAT	TAAAATTGAG	CGTGTGATTG	2150
GTGCAGGAGA	ATTTGGAGAA	GTTTGCAGTG	GTCGTTTGAA	ACTTCCGGGC	2200
CAGAGAGATG	TTGCAGTGGC	CATAAAAACC	CTGAAAGTTG	GTTACACAGA	2250

AAAGCAAAGG	AGGGACTTTT	TATGCGAAGC	AAGCATCATG	GGGCAATTTG	2300
ACCACCCAAA	TGTCGTCCAT	TTGGAAGGGG	TTGTTACAAG	AGGGAAGCCT	2350
GTCATGATTG	TGATAGAGTT	CATGGAGAAT	GGAGCCCTGG	ATGCATTTCT	2400
CAGGAAACAC	GATGGGCAGT	TTACAGTCAT	TCAGTTGGTA	GGAATGTTGA	2450
GAGGTATTGC	CGCTGGGATG	CGATACTTGG	CTGATATGGG	ATACGTTCAC	2500
AGGGACCTTG	CAGCGCGCAA	CATCCTTGTC	AACAGCAATC	TTGTTTGTAA	2550
AGTGTCAGAT	TTTGGCCTTT	CCCGGGTTAT	AGAGGATGAT	CCCGAAGCTG	2600
TCTACACCAC	GACTGGTGGA	AAAATTCCAG	TAAGGTGGAC	TGCACCGGAA	2650
GCCATTCAAT	ACCGGAAGTT	CACCTCAGCC	AGCGATGTGT	GGAGCTATGG	2700
GATTGTCATG	TGGGAAGTGA	TGTCTTATGG	AGAAAGACCT	TACTGGGACA	2750
TGTCAAATCA	AGATGTCATT	AAAGCGATAG	AAGAAGGTTA	TCGTTTGCCG	2800
GCGCCCATGG	ATTGCCCAGC	TGGTCTTCAC	CAGCTAATGC	TGGATTGTTG	2850
GCAGAAAGAT	CGGGCGGAAA	GGCCAAAGTT	TGAGCAGATA	GTCGGAATTC	2900
FAGACAAAAT	GATTCGAAAC	CCAAGTAGTC	TGAAAACACC	CCTGGGAACT	2950
TGTAGTAGAC	CCTTAAGCCC	TCTTCTGGAC	CAGAGCACTC	CTGACTTCAC	3000
PECCTTCTGT	TCAGTTGGAG	AATGGTTGCA	AGCTATTAAA	ATGGAAAGGT	3050
ATAAGGACAA	CTTCACAGCA	GCGGGTTACA	ACTCACTCGA	GTCAGTGGCC	3100
AGGATGACTA	TCGATGATGT	GATGAGTTTA	GGGATCACAC	TGGTTGGCCA	3150
TCAAAAGAAG	ATCATGAGCA	GCATCCAGAC	TATGCGGGCA	CAAATGTTGC	3200
ATTTACACGG	AACAGGCATC	CAAGTGTGAC	ACATCGGCCT	CCCTCAGATG	3250
AGGCTTAAGA	CTGCAGGAGA	ACAGTTCTGG	CCTTCAGTAT	ACGCATAGAA	3300
rgctgctaga	AGACAGTTGA	TATACTGGGT	CCTTCCTACA	AGAAAGAGAA	3350
GATTTTAGAA	GCACCTCCAG	ACTTGAACTC	CTAAGTGCCA	CCAGAATATA	3400
CAAAAAGGGA	ATTTAGGATC	CACCACTGGT	GGCCAGGAAC	ACAGCAGAGA	3450
CAATAAACAA	AGTACTACCT	GAAAAACATC	CCAACACCTT	GAGCTCTCGA	3500
ACCTCCTTTT	TATCTTATAG	ACTTTTTAAA	AATGTACATA	AAGAATTTAA	3550
GAAAGAATAT	ATTTGTCAAA	TAAAAATCAT	GATCTTATTG	TTAAAATCAA	3600
TGAAATATTT	TCCTTAAAAT	ATGTGATTTC	AGACTATTCT	TTTCCAGAAC	3650

CATCTGTGTT	TATTCTGCTT	AAGGACTTTG	TTTTAGAAAG	TTATTTGTAG	3700	
CTTTGGACCT	TTTTAGTGTT	AAATTTATGA	CACGTTACTA	CACTGGGAAC	3750	
CTTTGAAGAC	TCTCAAACTT	AAAGGAAAGC	AAAACTACGC	ACATAGTCGA	3800	
GGATGGACTT	TGTCCTTCAT	GGCTTTGGTA	TCCTGGCTGT	GTCATTTTGT	3850	
TAAACCAGTG	ATGTTTTCAT	ATTGTTTGCT	GATTGGCAGG	TAGTTCAAAA	3900	
TTGCAAGTTG	CCAAGAGCTC	TGATATTTT	TAACAGGATT	TTTTTTTCTT	3950	
TGTAAAAATC	AGATAACATA	CTAACTTTTC	AATGAAAAA	AAAAAAAAAG	4000	
AAGCAATAAT	GATCCATAAA	TACTATAAGG	CACTTTTAAC	AGATTGTTTA	4050	
TAGAGTGATT	TACTAGGCAG	AATTTAATAA	AAAAAAAAGA	GAGATGTCAA	4100	
ATTTTAGGTT	TATGTGTATA	TGATAAAAGG	CTGAGCTTCG	TCTGAAGATG	4150	
CTGGTGAAAG	CAAGACTGGA	AGCGAAGCTC	TCCAGCTTTG	GCTAACCCAA	4200	
TCCGAGCACA	TCAAGAGCTT	CAGTCTTGTG	ACAGTAAGAA	ATTTAGGAAC	4250	
ATAGTTGACC	TATATTTTGT	ATTCTTTCTT	GTTGAATGCA	GTCCAAATAC	4300	
AAAA					4304	
lak m						

INFORMATION FOR SEQUENCE ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:

998

(B) TYPE: (C) STRANDNESS: amino acid

(D) TOPOLOGY:

single linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Met Val Val Gln Thr Arg Phe Pro Ser Trp Ile Ile Leu Cys Tyr Ile 1 10 15

Trp Leu Leu Gly Phe Ala His Thr Gly Glu Ala Gln Ala Ala Lys Glu 20 2530

Val Leu Leu Asp Ser Lys Ala Gln Gln Thr Glu Leu Glu Trp Ile $\frac{35}{40}$

															,
Ser	Ser 50	Pro	Pro	Ser	Gly	Trp 55	Glu	Glu	Ile	Ser	Gly 60	Leu	Asp	Glu	Asn
Tyr 65	Thr	Pro	Ile	Arg	Thr 70	Tyr	Gln	Val	Cys	Gln 75	Val	Met	Glu	Pro	Asn 80
Gln	Asn	Asn	Trp	Leu 85	Arg	Thr	Asn	Trp	Ile 90	Ser	Lys	Gly	Asn	Ala 95	Gln
Arg	Ile	Phe	Val 100	Glu	Leu	Lys	Phe	Thr 105	Leu	Arg	Asp	Cys	Asn 110	Ser	Leu
Pro	Gly	Val 115	Leu	Gly	Thr	Cys	Lys 120	Glu	Thr	Phe	Asn	Leu 125	Tyr	Tyr	Tyr
Hu C	Thr 130	Asp	Tyr	Asp	Thr	Gly 135	Arg	Asn	Ile	Arg	Glu 140	Asn	Leu	Tyr	Val
ys 145	Ile	Asp	Thr	Ile	Ala 150	Ala	Asp	Glu	Ser	Phe 155	Thr	Gln	Gly	Asp	Leu 160
îly O	Glu	Arg	Lys	Met 165	Lys	Leu	Asn	Thr	Glu 170	Val	Arg	Glu	Ile	Gly 175	Pro
leu N	Ser	Lys	Lys 180	Gly	Phe	Tyr	Leu	Ala 185	Phe	Gln	Asp	Val	Gly 190	Ala	Cys
He	Ala	Leu 195	Val	Ser	Val	Lys	Val 200	Tyr	Tyr	Lys	Lys	Cys 205	Trp	Thr	Ile
Val	Glu 210	Asn	Leu	Ala	Val	Phe 215	Pro	Asp	Thr	Val	Thr 220	Gly	Ser	Glu	Phe
Ser 225	Ser	Leu	Val	Glu	Val 230	Arg	Gly	Thr	Cys	Val 235	Ser	Ser	Ala	Glu	Glu 240
3lu	Ala	Glu	Asn	Ser 245	Pro	Arg	Met	His	Cys 250	Ser	Ala	Glu	Gly	Glu 255	Trp
Leu	Val	Pro	Ile 260	Gly	Lys	Cys	Ile	Cys 265	Lys	Ala	Gly	Tyr	Gln 270	Gln	Lys
∃ly	Asp	Thr 275	Cys	Glu	Pro	Cys	Gly 280	Arg	Arg	Phe	Tyr	Lys 285	Ser	Ser	Ser
3ln	Asp 290	Leu	Gln	Cys	Ser	Arg 295	Cys	Pro	Thr	His	Ser 300	Phe	Ser	Asp	Arg
31u 305	Gly	Ser	Ser	Arg	Cys 310	Glu	Cys	Glu	Asp	Gly 315	Tyr	Tyr	Arg	Ala	Pro 320

Ser	Asp	Pro	Pro	Tyr 325	Val	Ala	Cys	Thr	Arg 330	Pro	Pro	Ser	Ala	Pro 335	Gln
Asn	Leu	Ile	Phe 340	Asn	Ile	Asn	Gln	Thr 345	Thr	Val	Ser	Leu	Glu 350	Trp	Ser
Pro	Pro	Ala 355	Asp	Asn	Gly	Gly	Arg 360	Asn	Asp	Val	Thr	Tyr 365	Arg	Ile	Leu
Cys	Lys 370	Arg	Cys	Ser	Trp	Glu 375	Gln	Gly	Glu	Cys	Val 380	Pro	Cys	Gly	Ser
Asn 385	Ile	Gly	Tyr	Met	Pro 390	Gln	Gln	Thr	Gly	Leu 395	Glu	Asp	Asn	Tyr	Val 400
Thr	Val	Met	Asp	Leu 405	Leu	Ala	His	Ala	Asn 410	Tyr	Thr	Phe	Glu	Val 415	Glu
Ala	Val	Asn	Gly 420	Val	Ser	Asp	Leu	Ser 425	Arg	Ser	Gln	Arg	Leu 430	Phe	Ala
Ala	Val	Ser 435	Ile	Thr	Thr	Gly	Gln 440	Ala	Ala	Pro	Ser	Gln 445	Val	Ser	Gly
val	Met 450	Lys	Glu	Arg	Val	Leu 455	Gln	Arg	Ser	Val	Gln 460	Leu	Ser	Trp	Gln
Glu 465	Pro	Glu	His	Pro	Asn 470	Gly	Val	Ile	Thr	Glu 475	Tyr	Glu	Ile	Lys	Tyr 480
Tyr	Glu	Lys	Asp	Gln 485	Arg	Glu	Arg	Thr	Tyr 490	Ser	Thr	Leu	Lys	Thr 495	Lys
Ser	Thr	Ser	Ala 500	Ser	Ile	Asn	Asn	Leu 505	Lys	Pro	Gly	Thr	Val 510	Tyr	Val
Phe	Gln	Ile 515	Arg	Ala	Val	Thr	Ala 520	Ala	Gly	Tyr	Gly	Asn 525	Tyr	Ser	Pro
Arg	Leu 530	Asp	Val	Ala	Thr	Leu 535	Glu	Glu	Ala	Ser	Gly 540	Lys	Met	Phe	Glu
Ala 545	Thr	Ala	Val	Ser	Ser 550	Glu	Gln	Asn	Pro	Val 555	Ile	Ile	Ile	Ala	Val 560
Val	Ala	Val	Ala	Gly 565	Thr	Ile	Ile	Leu	Val 570	Phe	Met	Val	Phe	Gly 575	Phe
Ile	Ile	Gly	Arg 580	Arg	His	Cys	Gly	Tyr 585	Ser	Lys	Ala	Asp	Gln 590	Glu	Gly
Asp	Glu	Glu 595	Leu	Tyr	Phe	His	Phe 600	Lys	Phe	Pro	Gly	Thr 605	Lys	Thr	Tyr

- Ile Asp Pro Glu Thr Tyr Glu Asp Pro Asn Arg Ala Val His Gln Phe
- Ala Lys Glu Leu Asp Ala Ser Cys Ile Lys Ile Glu Arg Val Ile Gly 625 630 630 640
- Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Pro Gly 645 655
- Gln Arg Asp Val Ala Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr $_{660}$ $_{660}$ $_{665}$
- Glu Lys Gln Arg Arg Asp Phe Leu Cys Glu Ala Ser Ile Met Gly Gln 675 680 685
- Phe Asp His Pro Asn Val Val His Leu Glu Gly Val Val Thr Arg Gly $_{\frac{1}{100}}$ 690 $\,$ 700
- Tys Pro Val Met Ile Val Ile Glu Phe Met Glu Asn Gly Ala Leu Asp 705 710 715 720
- Ha Phe Leu Arg Lys His Asp Gly Gln Phe Thr Val Ile Gln Leu Val 725 730 735
- Gly Met Leu Arg Gly Ile Ala Ala Gly Met Arg Tyr Leu Ala Asp Met 745 750
- अप Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser [4 755 हो।
- Msn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Ile Glu N 770 780
- Asp Asp Pro Glu Ala Val Tyr Thr Thr Thr Gly Gly Lys Ile Pro Val 785 790 795 800
- Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr Ser Ala 805
- Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr 820 825 830
- Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile Lys Ala 835 840 845
- Ile Glu Glu Gly Tyr Arg Leu Pro Ala Pro Met Asp Cys Pro Ala Gly 850 855 860
- Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Ala Glu Arg 865 870 875
- Pro Lys Phe Glu Gln Ile Val Gly Ile Leu Asp Lys Met Ile Arg Asn $885 \hspace{1.5cm} 890 \hspace{1.5cm} 895$

111 208/007

Pro Ser Ser Leu Lys Thr Pro Leu Gly Thr Cys Ser Arg Pro Leu Ser 900 905

Pro Leu Leu Asp Gln Ser Thr Pro Asp Phe Thr Ala Phe Cys Ser Val 920

Gly Glu Trp Leu Gln Ala Ile Lys Met Glu Arg Tyr Lys Asp Asn Phe

Thr Ala Ala Gly Tyr Asn Ser Leu Glu Ser Val Ala Arg Met Thr Ile 950 955 960

Asp Asp Val Met Ser Leu Gly Ile Thr Leu Val Gly His Gln Lys Lys

Ile Met Ser Ser Ile Gln Thr Met Arg Ala Gln Met Leu His Leu His je á

Thr Gly Ile Gln Val 995

PROBE.

INFORMATION FOR SEQUENCE ID NO:

(i) SEQUENCE CHARACTERISTICS:

> (A) LENGTH:

610

(B) TYPE:

amino acid

(C) STRANDNESS: (D)

single TOPOLOGY:

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:

Met Val Val Gln Thr Arg Phe Pro Ser Trp Ile Ile Leu Cys Tyr Ile

Trp Leu Leu Gly Phe Ala His Thr Gly Glu Ala Gln Ala Ala Lys Glu 20

Val Leu Leu Leu Asp Ser Lys Ala Gln Gln Thr Glu Leu Glu Trp Ile

Ser Ser Pro Pro Ser Gly Trp Glu Glu Ile Ser Gly Leu Asp Glu Asn

Tyr Thr Pro Ile Arg Thr Tyr Gln Val Cys Gln Val Met Glu Pro Asn 70

Gln Asn Asn Trp Leu Arg Thr Asn Trp Ile Ser Lys Gly Asn Ala Gln 90 Arg Ile Phe Val Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Val Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu Thr Asp Tyr Asp Thr Gly Arg Asn Ile Arg Glu Asn Leu Tyr Val Lys Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Gly Asp Leu Gly Glu Arg Lys Met Lys Leu Asn Thr Glu Val Arg Glu Ile Gly Pro Leu Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys the Ala Leu Val Ser Val Lys Val Tyr Tyr Lys Lys Cys Trp Thr Ile 195 ♥al Glu Asn Leu Ala Val Phe Pro Asp Thr Val Thr Gly Ser Glu Phe 210 Ser Ser Leu Val Glu Val Arg Gly Thr Cys Val Ser Ser Ala Glu Glu 235 Qu Ala Glu Asn Ser Pro Arg Met His Cys Ser Ala Glu Gly Glu Trp Leu Val Pro Ile Gly Lys Cys Ile Cys Lys Ala Gly Tyr Gln Gln Lys Gly Asp Thr Cys Glu Pro Cys Gly Arg Arg Phe Tyr Lys Ser Ser Ser Gln Asp Leu Gln Cys Ser Arg Cys Pro Thr His Ser Phe Ser Asp Arg Glu Gly Ser Ser Arg Cys Glu Cys Glu Asp Gly Tyr Tyr Arg Ala Pro Ser Asp Pro Pro Tyr Val Ala Cys Thr Arg Pro Pro Ser Ala Pro Gln Asn Leu Ile Phe Asn Ile Asn Gln Thr Thr Val Ser Leu Glu Trp Ser Pro Pro Ala Asp Asn Gly Gly Arg Asn Asp Val Thr Tyr Arg Ile Leu

Cys Lys Arg Cys Ser Trp Glu Gln Gly Glu Cys Val Pro Cys Gly Ser 370 375

Asn Ile Gly Tyr Met Pro Gln Gln Thr Gly Leu Glu Asp Asn Tyr Val 385 390 395 400

Thr Val Met Asp Leu Leu Ala His Ala Asn Tyr Thr Phe Glu Val Glu 405 410 415

Ala Val Asn Gly Val Ser Asp Leu Ser Arg Ser Gln Arg Leu Phe Ala 420 425 430

Ala Val Ser Ile Thr Thr Gly Gln Ala Ala Pro Ser Gln Val Ser Gly 435 440 445

Val Met Lys Glu Arg Val Leu Gln Arg Ser Val Gln Leu Ser Trp Gln $\frac{1}{450}$ 450 460

Hu Pro Glu His Pro Asn Gly Val Ile Thr Glu Tyr Glu Ile Lys Tyr 465 470 475 480

Tyr Glu Lys Asp Gln Arg Glu Arg Thr Tyr Ser Thr Leu Lys Thr Lys 485 490 495

Şer Thr Ser Ala Ser Ile Asn Asn Leu Lys Pro Gly Thr Val Tyr Val 510 500

the Gln Ile Arg Ala Val Thr Ala Ala Gly Tyr Gly Asn Tyr Ser Pro 515 520 525

 $\widehat{\mbox{Arg}}$ Leu Asp Val Ala Thr Leu Glu Glu Ala Ser Gly Lys Met Phe Glu 530 535 540

Ala Thr Ala Val Ser Ser Glu Gln Asn Pro Val Ile Ile Ile Ala Val 545 550 550 560

Val Ala Val Ala Gly Thr Ile Ile Leu Val Phe Met Val Phe Gly Phe 565 570 575

Ile Ile Gly Arg Arg His Cys Gly Tyr Ser Lys Ala Asp Gln Glu Gly 580 585 590

Asp Glu Glu Leu Tyr Phe His Ser Leu Val Thr Asn Glu His Leu Ser $595 \\ $ $600 \\ $ $605 \\ $

Val Leu 610

(1) INFORMATION FOR SEQUENCE ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2901

(B) TYPE: nucleic acid

(C) STRANDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: nucleic

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

AAGCGGCCGG TCTGCAGTCG GAGACTTGCA GGCAGCAAAC ACGGTGCGAA 50 CGAACCGGAG GGGGGAGAGA GAAATCAAAC AGCTAAGCGT GGAGCAGACG 100 GCCTGGGACC CAGAAGGGGA TCGATGCGAG GAGCGCAATA ATAACAACAA 150 TAATAACCCA CTTCGGAGCA AACAGCATCT AAAGAGCTGC GACCCAACTG 200 CAGCCTAAAA AAATCAAACC TGCTCATGCA CCATGGTTGT TCAAACTCGG 250 TTCCCTTCGT GGATTATTTT GTGTTACATC TGGCTGCTTG GCTTTGCACA 300 CACGGGGGAG GCGCAGGCTG CGAAGGAAGT ACTATTACTG GACTCGAAAG 350 CACAACAAAC AGAATTGGAA TGGATTTCCT CTCCACCCAG TGGGTGGGAA 400 GAAATTAGTG GTTTGGATGA GAACTACACT CCGATAAGAA CATACCAGGT 450 GTGCCAGGTC ATGGAGCCCA ACCAGAACAA CTGGCTGCGG ACTAACTGGA 500 TTTCTAAAGG CAACGCACAA AGGATTTTTG TAGAATTGAA ATTCACCTTG 550 AGGGATTGTA ATAGTCTTCC CGGAGTCCTG GGAACTTGCA AGGAAACGTT 600 TAATTTGTAC TATTATGAAA CAGACTACGA CACCGGCAGG AATATACGAG 650 AAAACCTTTA TGTTAAAATA GACACCATTG CTGCAGATGA AAGTTTCACA 700 CAAGGTGACC TTGGTGAAAG AAAGATGAAG CTGAACACTG AGGTGAGAGA 750 GATTGGACCT TTGTCCAAAA AGGGATTCTA TCTTGCCTTT CAGGATGTAG 800 GGGCTTGCAT AGCATTGGTT TCTGTCAAAG TGTACTACAA GAAGTGCTGG 850 ACCATTGTTG AGAACTTAGC TGTCTTTCCA GATACAGTGA CTGGTTCGGA 900 ATTTTCCTCC TTAGTCGAGG TCCGTGGGAC ATGTGTCAGC AGTGCCGAGG 950 AAGAGGCAGA AAATTCCCCC AGAATGCATT GCAGTGCAGA AGGAGAGTGG 1000 CTAGTACCCA TTGGAAAATG CATCTGCAAA GCAGGCTATC AGCAAAAAGG 1050

GGACACTTGC	GAACCCTGTG	GCCGCAGGTT	CTACAAATCT	TCCTCTCAGG	1100
ATCTCCAGTG	TTCTCGTTGT	CCAACCCACA	GCTTCTCTGA	CCGAGAAGGA	1150
TCATCCAGGT	GTGAATGTGA	AGATGGGTAC	TACAGAGCTC	CTTCTGATCC	1200
ACCATACGTT	GCATGCACGA	GGCCTCCCTC	TGCACCACAG	AACCTTATTT	1250
TCAATATCAA	TCAAACGACT	GTAAGTTTGG	AATGGAGTCC	TCCGGCTGAC	1300
AACGGGGGAA	GAAACGATGT	CACCTACAGA	ATACTGTGTA	AGCGGTGCAG	1350
TTGGGAACAG	GGAGAATGTG	TGCCATGCGG	AAGTAACATT	GGATACATGC	1400
CCCAGCAGAC	GGGATTAGAG	GATAACTATG	TCACTGTCAT	GGACCTACTT	1450
GCCCATGCAA	ATTACACTTT	CGAAGTTGAA	GCTGTAAATG	GAGTTTCGGA	1500
TTAAGCAGA	TCCCAGAGGC	TCTTCGCTGC	TGTTAGCATC	ACCACCGGTC	1550
AAGCAGCTCC	CTCGCAAGTG	AGTGGAGTCA	TGAAGGAGCG	AGTACTGCAG	1600
GGAGTGTGC	AGCTTTCCTG	GCAGGAGCCG	GAGCATCCCA	ATGGAGTCAT	1650
ACGGAATAT	GAAATCAAGT	ATTATGAGAA	AGATCAACGG	GAAAGGACGT	1700
TCAACACT	CAAAACCAAG	TCCACCTCCG	CCTCCATTAA	TAATCTGAAA	1750
eegggaacag	TGTACGTCTT	TCAGATCCGG	GCGGTCACTG	CTGCCGGTTA	1800
EGGAAACTAC	AGCCCTAGGC	TTGATGTTGC	CACACTTGAG	GAAGCTTCAG	1850
	TGAAGCGACA	GCAGTCTCCA	GTGAACAGAA	TCCTGTCATC	1900
ATAATTGCTG	TAGTGGCTGT	AGCAGGGACC	ATCATCTTGG	TGTTCATGGT	1950
STTCGGCTTC	ATCATTGGAA	GAAGGCACTG	TGGTTATAGC	AAGGCTGACC	2000
AGAAGGGGA	TGAAGAACTC	TACTTTCATT	CTTTAGTAAC	AAATGAGCAC	2050
CTGTCAGTTT	TATAAACCGC	AACAATAACT	GTTTAAGACA	ATCAATTTTG	2100
SATAAACAAT	CAACTACAGC	AGAATAAATC	AAGATTTTTA	AGTCCCATTT	2150
CCTTTATAC	ATTCTGCTTA	TTTTGTTGTT	ATATGTTTAT	TTTTTAAACT	2200
CTGATCTTGA	TTGAATGTGA	TACCATAAGC	ACAGTTAGGC	TGCAGTGTAA	2250
TATATAAAG	ACATTGTTCT	GAGAGCAGTA	CGATTTCATG	GAAAGATTGT	2300
TGGTGGCTT	TGTTAAAATT	AATAAAGAAT	TTTTAAGGAT	ATAGTGTAAT	2350
TTCTTCATT	GCATTAATAT	AACCAAATAT	GCCTACCTAT	CTTTGTCTTG	2400
ACCAAATGA	ATAGATTTGG	AATACTTTAT	TGTAATTGAA	TTTGATATAA	2450

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AGTTGACTGA GCATTTATGT GTTACCTGCA TGCTTCTGGG TGCATTGAAA 2500 TATTTTAACT TTTAAAATGA TACTATGTTG TTTCAATTTT GACTACCTTT 2550 TGTGAGGCAT ACTGGCTACC TCCTCCTATT AGCTAAGATC TTCCAAAGCC 2600 TTATAATGAA AAGTTTATAT AAACCATTTC TCTTTCAAAT CACTGTCATA 2650 CTTGGTCACG GATCCCAGGA ATATTGTAAA TTTTCTAATT TACTCTGCAC 2700 TTTGTATATC CAGCCTCTAT TACCCTCAAG GTGAATATAA AACTATGTCT 2750 TTTGAATATT TCTCTTTGAT TTTGTGATAG CAGTCCCTCA TATCTTGTAC 2800 TAATTTTATG TATATGTCAA CAGTGGTTGG TCTTTAAAAA TAAATCAAAG 2850 2900 ADTUCK . DELEC 2901

INFORMATION FOR SEQUENCE ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

> (A) LENGTH:

626

(B) TYPE: (C)

amino acid

STRANDNESS: (D) TOPOLOGY:

single linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:

Met Val Val Gln Thr Arg Phe Pro Ser Trp Ile Ile Leu Cys Tyr Ile

Trp Leu Leu Gly Phe Ala His Thr Gly Glu Ala Gln Ala Ala Lys Glu

Val Leu Leu Asp Ser Lys Ala Gln Gln Thr Glu Leu Glu Trp Ile

Ser Ser Pro Pro Ser Gly Trp Glu Glu Ile Ser Gly Leu Asp Glu Asn

Tyr Thr Pro Ile Arg Thr Tyr Gln Val Cys Gln Val Met Glu Pro Asn

Gln Asn Asn Trp Leu Arg Thr Asn Trp Ile Ser Lys Gly Asn Ala Gln 85

Arg Ile Phe Val Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu 100 Pro Gly Val Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu Thr Asp Tyr Asp Thr Gly Arg Asn Ile Arg Glu Asn Leu Tyr Val Lys Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Gly Asp Leu Gly Glu Arg Lys Met Lys Leu Asn Thr Glu Val Arg Glu Ile Gly Pro 170 Leu Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys de Ala Leu Val Ser Val Lys Val Tyr Tyr Lys Lys Cys Trp Thr Ile Val Glu Asn Leu Ala Val Phe Pro Asp Thr Val Thr Gly Ser Glu Phe 210 Ser Ser Leu Val Glu Val Arg Gly Thr Cys Val Ser Ser Ala Glu Glu 225 240 Glu Ala Glu Asn Ser Pro Arg Met His Cys Ser Ala Glu Gly Glu Trp 245 Leu Val Pro Ile Gly Lys Cys Ile Cys Lys Ala Gly Tyr Gln Gln Lys Gly Asp Thr Cys Glu Pro Cys Gly Arg Arg Phe Tyr Lys Ser Ser Ser Gln Asp Leu Gln Cys Ser Arg Cys Pro Thr His Ser Phe Ser Asp Arg 295 Glu Gly Ser Ser Arg Cys Glu Cys Glu Asp Gly Tyr Tyr Arg Ala Pro 305 320 Ser Asp Pro Pro Tyr Val Ala Cys Thr Arg Pro Pro Ser Ala Pro Gln 330 Asn Leu Ile Phe Asn Ile Asn Gln Thr Thr Val Ser Leu Glu Trp Ser 340 Pro Pro Ala Asp Asn Gly Gly Arg Asn Asp Val Thr Tyr Arg Ile Leu Cys Lys Arg Cys Ser Trp Glu Gln Gly Glu Cys Val Pro Cys Gly Ser

Asn Ile Gly Tyr Met Pro Gln Gln Thr Gly Leu Glu Asp Asn Tyr Val 390 Thr Val Met Asp Leu Leu Ala His Ala Asn Tyr Thr Phe Glu Val Glu Ala Val Asn Gly Val Ser Asp Leu Ser Arg Ser Gln Arg Leu Phe Ala Ala Val Ser Ile Thr Thr Gly Gln Ala Ala Pro Ser Gln Val Ser Gly Val Met Lys Glu Arg Val Leu Gln Arg Ser Val Gln Leu Ser Trp Gln Glu Pro Glu His Pro Asn Gly Val Ile Thr Glu Tyr Glu Ile Lys Tyr 465 480 Tyr Glu Lys Asp Gln Arg Glu Arg Thr Tyr Ser Thr Leu Lys Thr Lys 485 ser Thr Ser Ala Ser Ile Asn Asn Leu Lys Pro Gly Thr Val Tyr Val Phe Gln Ile Arg Ala Val Thr Ala Ala Gly Tyr Gly Asn Tyr Ser Pro Arg Leu Asp Val Ala Thr Leu Glu Glu Ala Ser Gly Lys Met Phe Glu Ala Thr Ala Val Ser Ser Glu Gln Asn Pro Val Ile Ile Ile Ala Val 545 560 Val Ala Val Ala Gly Thr Ile Ile Leu Val Phe Met Val Phe Gly Phe Ile Ile Gly Arg Arg His Cys Gly Tyr Ser Lys Ala Asp Gln Glu Gly 580 Asp Glu Glu Leu Tyr Phe His Ser Leu Tyr Arg Glu Arg Gly Asp Gly

Met Glu Lys Thr Gln His Asn Lys Lys Trp Met Ile Ala Ser Cys Ser

620

615

Arg Leu 625

(1) INFORMATION FOR SEQUENCE ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2323 (B) TYPE: nucleic acid (C) STRANDNESS: single

(C) STRANDNESS: single (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: nucleic

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

AAGCGGCCGG TCTGCAGTCG GAGACTTGCA GGCAGCAAAC ACGGTGCGAA 50 CGAACCGGAG GGGGGAGAGA GAAATCAAAC AGCTAAGCGT GGAGCAGACG 100 CCTGGGACC CAGAAGGGGA TCGATGCGAG GAGCGCAATA ATAACAACAA 150 TAATAACCCA CTTCGGAGCA AACAGCATCT AAAGAGCTGC GACCCAACTG 200 CAGCCTAAAA AAATCAAACC TGCTCATGCA CCATGGTTGT TCAAACTCGG 250 TTCCCTTCGT GGATTATTTT GTGTTACATC TGGCTGCTTG GCTTTGCACA 300 ACGGGGGAG GCGCAGGCTG CGAAGGAAGT ACTATTACTG GACTCGAAAG 350 CACAACAAAC AGAATTGGAA TGGATTTCCT CTCCACCCAG TGGGTGGGAA 400 GAAATTAGTG GTTTGGATGA GAACTACACT CCGATAAGAA CATACCAGGT 450 GTGCCAGGTC ATGGAGCCCA ACCAGAACAA CTGGCTGCGG ACTAACTGGA 500 TTTCTAAAGG CAACGCACAA AGGATTTTTG TAGAATTGAA ATTCACCTTG 550 AGGGATTGTA ATAGTCTTCC CGGAGTCCTG GGAACTTGCA AGGAAACGTT 600 TAATTTGTAC TATTATGAAA CAGACTACGA CACCGGCAGG AATATACGAG 650 AAAACCTTTA TGTTAAAATA GACACCATTG CTGCAGATGA AAGTTTCACA 700 CAAGGTGACC TTGGTGAAAG AAAGATGAAG CTGAACACTG AGGTGAGAGA 750 GATTGGACCT TTGTCCAAAA AGGGATTCTA TCTTGCCTTT CAGGATGTAG 800 GGGCTTGCAT AGCATTGGTT TCTGTCAAAG TGTACTACAA GAAGTGCTGG 850 ACCATTGTTG AGAACTTAGC TGTCTTTCCA GATACAGTGA CTGGTTCGGA 900 ATTTTCCTCC TTAGTCGAGG TCCGTGGGAC ATGTGTCAGC AGTGCCGAGG 950 AAGAGGCAGA AAATTCCCCC AGAATGCATT GCAGTGCAGA AGGAGAGTGG 1000 CTAGTACCCA TTGGAAAATG CATCTGCAAA GCAGGCTATC AGCAAAAAGG 1050

GGACACTTGC	GAACCCTGTG	GCCGCAGGTT	CTACAAATCT	TCCTCTCAGG	1100
ATCTCCAGTG	TTCTCGTTGT	CCAACCCACA	GCTTCTCTGA	CCGAGAAGGA	1150
TCATCCAGGT	GTGAATGTGA	AGATGGGTAC	TACAGAGCTC	CTTCTGATCC	1200
ACCATACGTT	' GCATGCACGA	GGCCTCCCTC	TGCACCACAG	AACCTTATTT	1250
TCAATATCAA	TCAAACGACT	GTAAGTTTGG	AATGGAGTCC	TCCGGCTGAC	1300
AACGGGGGAA	GAAACGATGT	CACCTACAGA	ATACTGTGTA	AGCGGTGCAG	1350
TTGGGAACAG	GGAGAATGTG	TGCCATGCGG	AAGTAACATT	GGATACATGC	1400
CCCAGCAGAC	GGGATTAGAG	GATAACTATG	TCACTGTCAT	GGACCTACTT	1450
GCCCATGCAA	ATTACACTTT	CGAAGTTGAA	GCTGTAAATG	GAGTTTCGGA	1500
CTTAAGCAGA	TCCCAGAGGC	TCTTCGCTGC	TGTTAGCATC	ACCACCGGTC	1550
AAGCAGCTCC	CTCGCAAGTG	AGTGGAGTCA	TGAAGGAGCG	AGTACTGCAG	1600
CCGAGTGTGC	AGCTTTCCTG	GCAGGAGCCG	GAGCATCCCA	ATGGAGTCAT	1650
CACGGAATAT	GAAATCAAGT	ATTATGAGAA	AGATCAACGG	GAAAGGACGT	1700
ACTCAACACT	CAAAACCAAG	TCCACCTCCG	CCTCCATTAA	TAATCTGAAA	1750
CCGGGAACAG	TGTACGTCTT	TCAGATCCGG	GCGGTCACTG	CTGCCGGTTA	1800
174		TTGATGTTGC			1850
		GCAGTCTCCA			1900
		AGCAGGGACC			1950
		GAAGGCACTG			2000
		TACTTTCATT			2050
		GCACAATAAG			2100
		TTCCTAATCA			2150
		AAGAGATAAG			2200
		AAAGAGATGA			2250
		TCTTTTTTGA	TAATTAGTGC	TCAGGGGAGG	2300
GGGGGGAAG	TAGAGAAAGC	AAA			2323

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(2) INFORMATION FOR SEQ ID NO: 7:
   (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH:
        (B) TYPE:
                                 amino acid
        (C) STRANDEDNESS:
                                 single
        (D) TOPOLOGY:
                                  linear
   (ii) MOLECULE TYPE:
                                peptide
   (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:
Ala Ala Thr Ala Ala Ala
(2) INFORMATION FOR SEQ ID NO: 8:
  (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH:
        (B) TYPE:
                                amino acid
        (C) STRANDEDNESS:
                                single
        (D) TOPOLOGY:
                                 linear
  (ii) MOLECULE TYPE:
                                peptide
   (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:
Ala Ala Thr Ala Ala Ala
                5
(2) INFORMATION FOR SEQ ID NO: 9:
   (i) SEOUENCE CHARACTERISTICS:
        (A) LENGTH:
        (B) TYPE:
                                 amino acid
        (C) STRANDEDNESS:
                                 single
        (D) TOPOLOGY:
                                 linear
   (ii) MOLECULE TYPE:
                                 peptide
   (xi) SEQUENCE DESCRIPTION: SEO ID NO: 9:
His Arg Asp Leu Ala Ala
                5
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(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

(B) TYPE: (C) STRANDEDNESS:

amino acid single

(D) TOPOLOGY:

linear

(ii) MOLECULE TYPE:

peptide

(ix) FEATURE:

(D) OTHER INFORMATION:

Xaa in position 2 is valine or methionine; Xaa in position 5 is

phenylalanine or tyrosine.

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Asp Xaa Trp Ser Xaa Gly

TUBERT DETRUE